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APPLICATION NO. 08/474,338	FILING DATE 07/07/95	FIRST NAMED INVENTOR SPRINGER	ATTORNEY DOCKET NO. 000

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EXAMINER CUNNINGHAM, T	
ART UNIT 1816	PAPER NUMBER

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 08/474,388	Applicant(s) Springer et al.
	Examiner Thomas M. Cunningham	Group Art Unit 1816

☒ Responsive to communication(s) filed on *Jan 7, 1997*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *71-86* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *71-86* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. The prior restriction requirement is withdrawn. Claims 71-86 are subject to examination.

2. Applicant is required to verify and update the status of priority applications enumerated by page 1 of the specification.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as the invention.

4. Claims 71-86 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The term "ICAM-1" when read in light of the specification has been interpreted as being limited to full-length, transmembrane human intercellular adhesion molecule 1, e.g. residues 1-505 as described in Fig. 8.

B. In claims 71 and 80 it is unclear what the scope of the term "natural contaminants" is. Is this limited to cellular components found in human cells which express ICAM-1? Does this term encompass contaminants from prokaryotic or eukaryotic cells which have been engineered to express ICAM-1?

C. In claims 73 and 81 it is unclear what the scope of the term "bind lymphocytes" of "lymphocyte binding" is. Is this term limited to known ICAM-1 specific ligands like LFA-1 or does it generally encompass molecules such as lipids in the cell membrane to which the transmembrane domain of the molecule of ICAM-1 associates? Does it exclude binding to molecules like T cell receptors or T cell receptor accessory molecules like CD4 and CD8?

D. In claims 71, 80, 81, and 84-86 it is unclear what the scope of the terms "biological activity" or "biologically active" are. Are these terms limited to the ability of ICAM-1 to bind to HRV or LFA-1? Do they encompass immunological or antigenic activity, e.g. the ability to induce or be bound by an antibody?

E. In claims 79 and 83 the term "has" has been interpreted as being open claim language comparable to "comprises".

F. In claims 75-78 the term "about" is vague and indefinite.

(1) Is this term limited to 1%, 5%, 10%, 100% or less variation in the recited molecular masses? Where is it defined in the specification?

(2) Is this intended to encompass a family of native ICAM-1 molecules with slightly different molecular masses as purified, e.g. by virtue of different degrees of glycosylation or expression of alternatively processed mRNA transcripts?

(3) Is there another limitation that would serve to define this mass range more clearly? An accused infringer would interpret this term differently than a patent holder. Therefore, clarification is required.

G. In claims 71-79 it is unclear what the term "preparation" encompasses or excludes. Does this term require that the ICAM-1 product be produced by a particular preparative method or from a particular source, e.g. from natural sources such as cell lines

like human spleen cells or JY cells? Is this term limited to ICAM-1 alone or does it include compositions comprising ICAM-1 and an excipient or carrier (e.g. a composition)?

H. In claims 80-83 it is unclear what the scope of the term "lipid membrane" is. Is this limited to lipid bilayers formed of naturally-occurring phospholipids, sphingolipids or cholesterols? Does this term embrace ICAM-1 in detergent solutions or micelles? Does his term embrace liposomes?

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 71-86 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art

to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A. The specification only describes ICAM-1 having the sequence set forth by Fig. 8. No other amino acid sequences for native ICAM-1 products with different sequences are described.

B. The specification does not adequately describe which preparations of ICAM-1 retain particular biological properties such as the ability to bind to LFA-1, lymphocytes or HRV.

C. The specification only describes particular molecules on the surfaces of lymphocytes, such as LFA-1 or members of the LFA-1 family (CD11/CD18), which bind to ICAM-1.

D. Claims 80-83 are rejected under 35 U.S.C. 112, first paragraph as being enabled only for those forms of ICAM-1 products, lipid membranes and methods of incorporation dislosed on pages 85-87 of the specification. Different products and methods would be expected to result in lipid-incorporated ICAM-1

with materially different products. For instance, use of different domains of ICAM-1 would impart different binding characteristics. Use of different types of lipids would result in different stabilities and configurations of ICAM-1 within a membrane and result in a product with unpredictable stability, bioavailability and binding properties.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. Claims 71-79, 84 and 86 are rejected under 35 U.S.C. 102(a) or (b) over Dustin et al., J. Immunology 137:245 (July 1, 1986). These claims are directed to ICAM-1 preparations from JY cells, human spleenocytes or myelomonocytic cells. Page 66 of the specification refers to Dustin et al. The abstract of this publication indicates that ICAM-1 displays Mr heterogeneity depending on the cell type from which it is isolated. The nonglycosylated form of ICAM-1 is taught to have an Mr of 55,000 Da.

The claims recited above all embrace forms of ICAM-1 that are identical to those taught by Dustin et al. I.e. the claims encompass ICAM-1 recombinantly-produced in cell lines which would provide the same type of glycosylation as the native cell lines taught by Dustin et al.

9. Claims 71-79, 84 and 86 are rejected under 35 U.S.C. 102(e) as being anticipated by Greve, U.S. patent 5,589,453 (priority to 9/1/88). The cited patent, columns 4-7, teaches human rhinovirus receptor protein (now referred to as ICAM-1) prepared from HeLa cells with an Mr of about 95,000 Da and tryptic fragments of

ICAM-1. Claims 71-74 are anticipated because the prior art HRRP (ICAM-1) would inherently have the biological activities of native ICAM-1, such as antigenicity, ability to bind LFA-1, lymphocytes or HRV. Greve specifically teaches that ICAM-1 binds to HRV, see e.g. claims. The molecular mass limitations of claims 75-78 are anticipated by the HRRP (ICAM-1) of Greve et al because the 95,000 Da ICAM-1 protein of Greve has been interpreted as being "about" 72-91 kDa, 76.5-97 kDa, 114 kDa and 97 kDa thus meeting the limitations of claims 75-78. HRRP of Greve (ICAM-1) would inherently have the amino acid sequence of Figure 8, thus meeting the limitation of claim 79. The eukaryotically-expressed ICAM-1 of claims 84 and 86 embraces the 95,000 Da HRRP (ICAM-1) of Greve.

The lipid membranes comprising isolated of purified ICAM-1 of claims 80-83 are anticipated by the detergent-isolated ICAM-1 of Greve. Detergent isolated ICAM-1 would be complexed with hydrophobic detergent moieties in membranous micellar forms and would inherently retain the functional binding activities of the native molecule as evidenced by Greve's disclosure that it binds HRV.

Claim 85 has not been rejected as being anticipated because a prokaryotically-expressed ICAM-1 protein would lack the glycosylation of the ICAM-1 of Greve.

10. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order

for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

12. Claims 71-79 and 84-86 are rejected under 35 U.S.C. 102(a) or (b) as being anticipated by, or alteratively under 35 U.S.C. 103(a) as being unpatentable over Staunton et al., Cell 52:925-933 (March 25, 1988), or Tomassini et al., PNAS 86:4907-4911 (July, 1989).

Each of these documents describes expression of ICAM-1 products by cloning the DNA encoding ICAM-1. To the extent that the instant claims read ICAM-1 proteins encoded by the DNA sequences set forth by Fig. 2 of Staunton et al., Fig. 3 of Tomassini et al. (PNAS, 1988) these documents appear to anticipate the instant invention.

The instant claims also encompass variants or fragments of ICAM-1 sequences. One with ordinary skill in the art at the time of invention would have been motivated to make and use such fragments and variants corresponding to the functionally active sites of ICAM-1 based on the rDNA methods taught by these references, in view of the disclosure by Staunton et al. of anti-

ICAM-1 antibodies which block particular functional activities of the molecule. Such antibodies would be able to pick out which ICAM-1 fragments have useful functional activities such as blocking cellular adhesion interactions or inducing antibodies useful in identification of ICAM-1 products.

13. Claims 80-83 are rejected under 35 U.S.C. 102(a) or (b) as being anticipated by, or alteratively under 35 U.S.C. 103(a) as being unpatentable over Staunton et al., Cell 52:925-933 (March 25, 1988), or Tomassini et al., PNAS 86:4907-4911 (July, 1989) and further in view of the admitted prior art on page 86 of the specification: Gay et al. or Brain et al.

The production of ICAM-1 has been discussed above. It would have been prima facie obvious to one of ordinary skill in the art at the time of invention incorporate ICAM-1 products into lipid membranes or planar membranes for the purpose of enhancing its ability to attach to solid supports for diagnostic use or for the purpose of slowing its release and thus increasing its immunogenicity or bioavailability.

14. Papers related to this application may be submitted to Group 1800 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Thomas Cunningham, Art Unit 1816 and should be marked either "OFFICIAL" for entry into the prosecution history or "DRAFT" for consideration by the Examiner without entry. The Art Unit 1816 FAX telephone number is (703) 305-7939. FAX machines will be available to receive transmissions 24 hours a day.

15. In compliance with 1096 OG 30 the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or federal holiday with the District of Columbia, in which case the official date of receipt will be the next business day.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas M. Cunningham, Ph.D, J.D. whose telephone number is (703) 308-3968.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

THOMAS M. CUNNINGHAM
PRIMARY EXAMINER
GROUP 1800